

Award Number: DAMD17-02-1-0324

TITLE: Monitoring the Response of Chemotherapy on Breast
Cancer Tumors by Photon Migration Spectroscopy

PRINCIPAL INVESTIGATOR: David J. Hsiang, M.D.

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REPORT DATE: June 2003

TYPE OF REPORT: Annual Summary

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
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20031112 155

REPORT DOCUMENTATION PAGEForm Approved
OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE June 2003	3. REPORT TYPE AND DATES COVERED Annual Summary (6 May 02 - 5 May 03)	
4. TITLE AND SUBTITLE Monitoring the Response of Chemotherapy on Breast Cancer Tumors by Photon Migration Spectroscopy			5. FUNDING NUMBERS DAMD17-02-1-0324	
6. AUTHOR(S) David J. Hsiang, M.D.				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of California, Irving Irvine, California 92697-1875 E-Mail: dhsiang@uci.edu			8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSORING / MONITORING AGENCY REPORT NUMBER	
11. SUPPLEMENTARY NOTES Original contains color plates: All DTIC reproductions will be in black and white.				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited				12b. DISTRIBUTION CODE
13. ABSTRACT (Maximum 200 Words) Optimal management of patients with locally advanced breast cancer (LABC) remains a complex therapeutic problem. LABC represents 5-20 % of all newly diagnosed breast cancers in the United States with a higher incidence in medically underserved areas. Over the years, treatment for LABC has been evolving from radical mastectomy to the use of neoadjuvant chemotherapy followed with mastectomy or breast conservation therapy. The optimal intensity and duration of neoadjuvant chemotherapy for LABC still remains controversial due to the difficulty of evaluating response to therapy. Presently, response to treatment is measured by physical exam, mammography and or ultrasound. Several studies have showed significant discrepancies between the clinical assessment of response to neoadjuvant chemotherapy and the pathologic assessment of response found in post therapy surgical specimens. The goal of this project is to use Photon Migration Spectroscopy (PMS) as a new modality to monitor the response of breast tumor to neoadjuvant chemotherapy. PMS has shown excellent sensitivity to crucial early functional changes in breast tissue subjected to neoadjuvant chemotherapy which can be pivotal to the choice of chemotherapy agents and final survival outcome.				
14. SUBJECT TERMS Neoadjuvant Chemotherapy. Photomedicine. Laser Imaging				15. NUMBER OF PAGES 19
				16. PRICE CODE
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

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INTRODUCTION

Optimal management of patients with locally advanced breast cancer (LABC) remains a complex therapeutic problem. LABC represents 5-20 % of all newly diagnosed breast cancers in the United States with a higher incidence in medically underserved areas. Over the years, treatment for LABC has been evolving from radical mastectomy to the use of neoadjuvant chemotherapy followed with mastectomy or breast conservation therapy. The optimal intensity and duration of neoadjuvant chemotherapy for LABC still remains controversial due to the difficulty of evaluating response to therapy. Presently, response to treatment is measured by physical exam, mammography and or ultrasound. Several studies have showed significant discrepancies between the clinical assessment of response to neoadjuvant chemotherapy and the pathologic assessment of response found in post therapy surgical specimens. The goal of this project is to use Photon Migration Spectroscopy (PMS) as a new modality to monitor the response of breast tumor to neoadjuvant chemotherapy. Thus far Photon Migration Spectroscopy has shown excellent sensitivity to the crucial early functional changes in breast tissue subjected to neoadjuvant chemotherapy which can be pivotal to the choice of chemotherapy agents and final survival outcome.

BODY

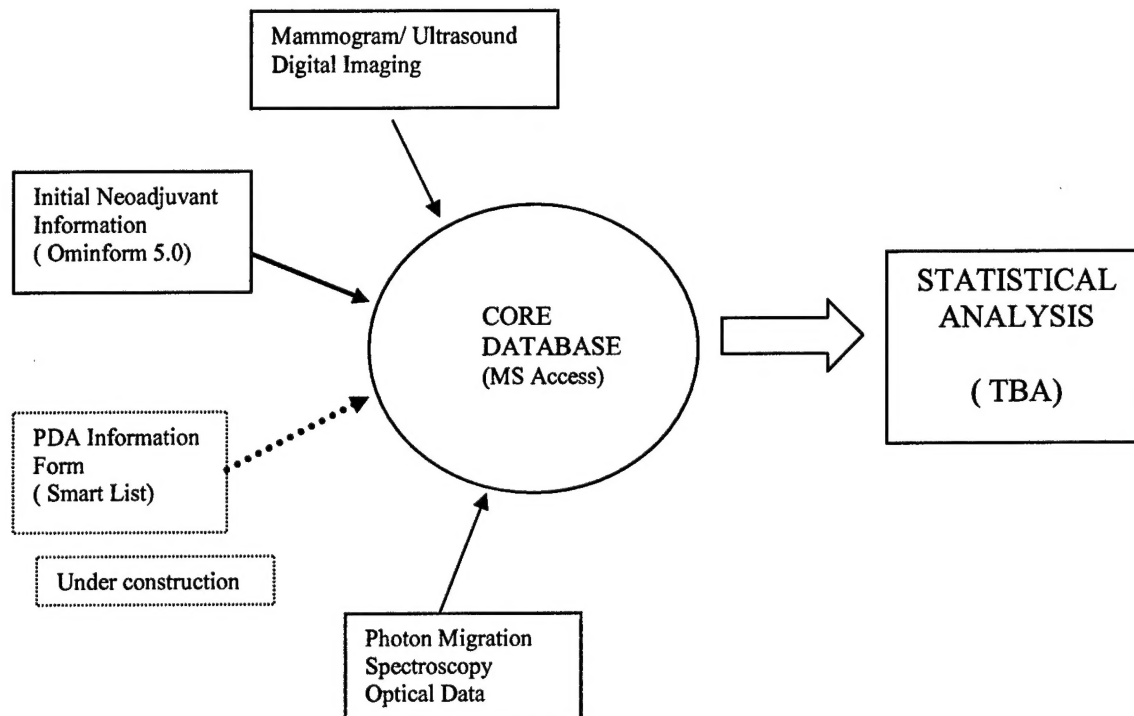
Statement of Work Accomplishments

SPECIFIC AIM 1: DEVELOP TRIAL PROTOCOL

1/2. Develop subject tracking system / Design Database

These tasks have been completed. It is very important to develop a database to manage the large amount of clinical data that will be generated in this study. Many systems were investigated. All had their strength and weakness. It was finally decided that the database would be composed of several units. Taking time to design and program a custom database would not be practical and may delay implementation of the system. The database system will be composed of several commercial products based on a Microsoft Access core. The data entry would be a specialized data collection form constructed by using Ominform 5.0 . (Refer to appendix A) . This form is used initially to record all vital statistics on the patient. This can then be exported to a MS Access database. The core is based on the MS Access software because of its flexibility at generating reports and querying capabilities. The original proposal of developing a Palm PDA based software is still being considered. The data collection form can be ported over to the PDA platform, but the screen size of the Palm PDA maybe inadequate. We are looking into working with the PC Tablet platform.

Below is a flowchart of the data entry



3. Submit application for IRB approval of clinical trial

This task has been completed. After receiving confirmation of funding for project an application was submitted to the University's Institutional Review Board. This was approved on 4/10/2002. Since then the protocol has been review and approved for another year until 2004. (Refer to appendix B).

4. Decide on optimal scanning parameters.

This task has been completed. It was important to find the ideal parameters for the scanners. The data to determine this was based on previous scans. Consideration was given to several factors: wavelength, duration of scan, number of repeat scanning, scanning grid, and total time of scan, patient comfort and reliability of data. The following is our current scanning parameters. *"Subject will have PMS measurements obtained at the tumor site, the contra lateral breast, and abdominal wall. All measurements will be performed using a non-invasive, diode-laser-based PMS device optimized for clinical optical property studies. The system employs up to 6 NIR (660nm to 850nm) wavelengths and multiple modulation frequencies (3 kHz-1GHz). Data is acquired using a hand-held scanning probe. The probe incorporates a source-detector pair 2.8 cm in separation. Each measurement is 45 sec in duration and is repeated 2X."*

This scanning parameter is also continuously being evaluated and any important changes will be reported to the DOD research committee.

SPECIFIC AIMS 2 : TRAINING

1. *Audit Bioengineering ,Physics and Photomedicine courses on campus to enhance fundamental knowledge of Photon Migration Spectroscopy*

This task has started and continues. Since this career move involves the understanding of optics and its physical properties, I have taken the opportunity to audit several Photomedicine and Physic course offered on campus. Due time and requirement constraints I have not formally enrolled in the classes. I have also made it a habit to attend a series of lunch time lecture given at the Beckman Laser Institute covering the field of laser and optics. The range of topic varies widely and is very interesting. (Refer to appendix C) By attending these lectures it introduces me to new concepts which can lead to further projects. One example is when I attended a lecture on Laser and removal of nevi and portwine stains. In this lecture the concept of Q switch lasers was introduced and how by adjusting the frequency and wavelength these lasers can specifically destroy melanocytes in skin. I am currently writing a new grant based on this principle by using the Q switch laser and obtaining clear margins on melanoma. The ideal would be to use this type laser on the surgical margins of melanoma and decrease the size of the excision needed in traditional surgery. The clinical benefits would be tremendous especially for melanomas on the face/lips where excisions can cause great disfiguration and handicaps.

2. *Rotation in Pathology department to learn slide preparation and immunohistochemical staining*

This task has been completed. I was able to observe and learn how to prepare slides of breast tissue. This was informative in that it showed me the techniques and how they can affect the final outcome. I have also worked with Dr. Lin on how to read breast tissue slides. I think this was informative but I think for the rest of the project I will not personally prepare the slides because it is too labor intensive and the lab techs can do a very good job.

3. *Enrollment in Ultrasound training course*

This task is currently being completed. The issue of enrolling for an ultrasound training course was a bit more complicated than first planned. The course was 2 years in length and was prohibitively expensive. Thus I have presently not enrolled in a course. Another problem we ran into was the obtaining ultrasound images of the breast tumor. Most insurance companies will not allow for an ultrasound to be obtained on the patients if they had a mammogram. In addition, the radiology department would not perform the study with no cost. But as luck would have it, one of the breast cancer patients (not neoadjuvant) donated \$50,000.00 to buy a dedicated portable ultrasound machine which we can use for the project. As a result, we will be obtaining a dedicated portable ultrasound machine (Sonosite 180 Plus) in July 2003 and the equipment seller will be providing me and my research partners a course in ultrasound equipment use.

SPECIFIC AIMS 3: ENROLLMENT OF SUBJECTS

1. Start enrollment of subjects

This task has been started and continues. When we first proposed this project, there was always the question of whether we would be able to accrue the number of patients needed. Based on historical data obtained from the Tumor Registry at UCI it was estimated that UCI sees about 12-14 locally advanced breast cases per year. Thus it was estimated that we would be able to accrue 12 per year. This was an ambitious target. I am happy to report that since we started to accrue 6/2003 we have been able to accrue 8 patients over the 12 month period. We approached a total of 11 patients. Our accrual rate is 73% . The reasons that the 3 patients that did not want to participate varied from the time involved, no interest and seeking treatment at another institution. We are also asking help from the community surgeons/oncologists in local areas to help recruit patients. Hopefully as this program develops our referral numbers will increase. (See Appendix D)

2. Scheduling of subsequent measurement dates

This task has been started and continues. Since the enrollment of the subjects we have been actively measuring the changes in the breast tumor receiving neoadjuvant chemotherapy. Originally it was planned to obtain 4 readings per cycle. We have been able to achieve more readings in the initial cycles but as the treatment continues the patients get weak and miss more of their appointments. This is not a big issue because with the preliminary data suggest the largest change is usually after the first treatment and the changes become more subtle in the subsequent cycles. This correlates with our theory that PMS is sensitive to breast tumor changes **early** in treatment which is important in the case of a nonresponder where one may need to change chemotherapy agents.

SPECIFIC AIMS 4 : TUMOR MEASUREMENTS

1. Obtain Pre - Post Chemotherapy Photon Migration Spectroscopy measurements

This task has been started and continues. Please refer to Specific Aim 3 Task 2 for comments. (Refer to appendix E)

2. Obtain Pre - Post Chemotherapy Ultrasound measurements

This task is delayed and will start in July 2003. Please refer to reason in Specific Aim 2 Task 3 for comments.

SPECIFIC AIMS 5 : CORRELATION OF PMS MEASUREMENTS WITH ULTRASOUND AND HISTOLOGY DATA

1. Correlation of Ultrasound data and PMS data

This task is pending.

2. Analysis of histology data with immunohistological staining of post surgical specimens

This task is pending.

SPECIFIC AIMS 6 : FINAL ANALYSIS AND REPORT

1. Analysis of all data

This task is pending.

2. Preparation of manuscript

This task is pending.

KEY RESEARCH / CAREER ACCOMPLISHMENTS

1. Development of database for data management
2. Development of trial protocol
3. Obtaining IRB approval of protocol
4. Audit of Photomedicine / Optic courses
5. Rotation in Pathology lab
6. Enrollment of subjects
7. Preliminary Photon Migration Data on Neoadjuvant Chemotherapy subjects

REPORTABLE OUTCOMES

1. Due to this Career Development Award I was able to generate several additional projects and obtain funding:

A) Avon Research Grant. The title of the grant is "*Correlative study of Photon Migration Spectroscopy measurements and Angiogenesis in Breast cancer tumors*". The project is to develop animal models with breast cancer tumors and subject them to various chemotherapy agents while performing PMS measurements on the tumor. This model would give us more

flexibility on testing measuring parameters and correlations with tissue histology than with human subjects. (Amount \$18,550)

B) Beckman Laser Institute Biomedical Engineering Fellowship. Wendy Tanamai a UCI 3rd year student received a fellowship to work on the Avon Research Grant. She will be performing the research work over the summer . (Amount \$4,000)

2. Presentation

Presented the preliminary data at Avon Foundation Breast Cancer Research and Care Symposium., November 16-19 2002 Emory University, Atlanta , Georgia

3. Collaborations

A) Recently, I have collaborated with the Epidemiology Division at UCI to submit a large Project Program Grant for Evaluating High Risk Breast Cancer Women. There were a total of 4 projects and I was Principle Investigator on Project 3. I was going to use the Photon Migration Spectroscopy (PMS) to evaluate the physiological changes in 400 high risk women over a 5 year period. This would be correlated with the other projects looking molecular marker and mammographic density. We had our site visit in January and now we are submitting our rebuttals. (Estimate 3-4 Million for PMS section - Total PPG 12 Million)

B) In March 2003 I have also started a collaborative project with UCSF by using the Photon Migration Spectroscopy concurrently with MRI scanning of subjects undergoing Neoadjuvant chemotherapy. We are sharing information and there has been very exciting data generated from this collaboration.

CONCLUSIONS

In summary , I think the career development grant is going well. It has provided me with support by which I have been able to obtain other grants and collaborate with other investigators. I do not think my progress would have been possible without this career grant. The protected time has been invaluable. Trying to switch over from a clinical to research career path has definitely not been easy. Just the simple task of writing a protocol and getting it approved by the IRB was a challenge. One almost has to learn a new way of thinking and processing information. But I am enjoying this change and feel confident I will succeed.

Although, I have not published any papers thus far, my plan is to start writing a paper based on some of the preliminary data we have so far. All the preliminary data show that PMS is very sensitive to the changes in breast tumor physiology to neoadjuvant therapy. But I still need to analyze the data on several subjects that have not responded to chemotherapy (i.e. non-responder) and patients that change chemotherapy agents mid cycle. I think information about these subjects will be key because it is actually the non-responders that we need to identify early and change their agents appropriately to optimize their treatment.

I look forward to next year's report when I will be able to present the data and any conclusions.

APPENDICES

- A. Questionnaire for patients in Optical studies of breast tissue (sample)
- B. Institutional Review Board - approval form
- C. Beckman Laser Institute Lecture Series
- D. Subject enrollment list
- E. Preliminary Optical Data

Patient ID 2306#1

Date 6/18/02

Appendix A






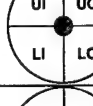
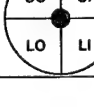
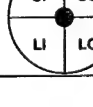


Questionnaire for patients in optical studies of breast tissue

The purpose of this questionnaire is to gather important information that is believed to affect the breast. This information is meant for *research purposes only*, and will *not* be available for sale, distribution, or public viewing. Only research personnel and the appropriate authorities as required by law have access to this questionnaire. Your identity will not be revealed. This questionnaire is not meant to provide you with any detailed information about your present or future health.

Please answer these questions as well as possible, either by filling in the appropriate response, or by checking the appropriate box. Thank you for your assistance

General Information					
Age	Wt	Ht	Bra size	Race	Skin color
49 yrs.	147 lbs.	5'5' ft'in"	A D B E C X —	white asian X black hispanic	light medium X dark

History of Breast Cancer			
Family or Relative	at age	Treatment	Survival
NONE		yes	yes
	yrs	no unk	no unk
		yes	yes
	yrs	no unk	no unk
		yes	yes
	yrs	no unk	no unk

Exam History				
Please refer to the diagram below. Please circle a location as appropriate. Please include information from your last exam.				
Exam	Date	Finding	Right	Left
Mammogram	5/21/02	normal abnormal X		
Physical exam	/ /	normal abnormal		
Ultrasound	5/21/02	normal abnormal X		
MRI	5/ 22/02	normal abnormal X		
Other than listed above, have you ever had an abnormal mammogram? yes no X				
If so, please indicate date and location	date / /			

Medication History			
Medication	Start	End	
oral contraceptive	1982	1983	
estrogen (i.e., HRT)			
progesterone (i.e., HRT)			
tamoxifen			
raloxifene			
coumadin			
cholestyramine			
androgens (male hormones)			
erythropoietin (EPO)			
chemotherapy agents			
other			
other			

Pregnancy History			
Number of pregnancies (include miscarriages)	# 1	Have you ever breast fed	yes no X
Number of live births	# 1	Are you currently breast feeding?	yes no X
Age at first live birth	34 yr	How long did you breast feed (total time in months)?	mo.
Date of last birth	12/8/88		
Are you currently pregnant?	yes no X		

Gynecological History		
Please check one box and fill in the question to the right.		
X Pre-menopausal	First day of last menstruation?	6/4/02
Post-menopausal	Date stopped?	
Peri-menopausal	Date of irregularity?	

breast tenderness & swelling ?	none X mild severe
menstrual cycle regularity?	X regular irregular
menstrual cycle length (i.e. 28)?	28 days

Patient ID ____2306#1

Date ____6/18/02

Appendix A**Medical History**

condition	yes or no	start date	end date
heart disease	yes no X		
hypertension	yes no X		
stroke	yes no X		
high cholesterol	yes no X		
diabetes	yes no X		
breast infection	yes no X		

condition	yes or no	start date	end date
breast injury/burns	yes no X		
anemia	yes no X		
sickle cell	yes no X		
hemophilia	yes no X		
blood clots	yes no X		
other			

Surgical History

procedure	yes or no	site	
mastectomy	yes no X	right left	
breast implant	yes no X	right left	silicone saline

procedure	yes or no	date
hysterectomy	yes no X	
oophorectomy	yes no X	

If you have had multiple procedures, please indicate on additional charts as necessary.

procedure	yes or no	number	dates	Right	Left	notes
lumpectomy	yes no X	#				
needle biopsy	yes no X	#				
CORE biopsy			5/31/02			RUI

Additional Comments

Please sign the questionnaire once you have completed it. Thank you very much for your time.

Print name _____

Signature _____

Date ____6/18/02____

Patient ID 2306#1/563-#119

Protocol number **Appendix A**

Neoadjuvant procedure for patients in optical studies of breast tissue

Date of First Chemotherapy 6/19/02

Physical Exam				Pregnancy Test			
Exam	Date	tumor size	Right Left	Urine test	yes no	Neg Pos	Date
Physical exam	5/21/02	____ in 3.5 x 4 ____ cm	<div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> RUI </div> <div style="text-align: center;"> </div> </div>				
Physical exam	/ /	____ in ____ cm	<div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> </div> <div style="text-align: center;"> </div> </div>				
Physical exam	/ /	____ in ____ cm	<div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> </div> <div style="text-align: center;"> </div> </div>				
Physical exam	/ /	____ in ____ cm	<div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> </div> <div style="text-align: center;"> </div> </div>				
Comment CORE biopsy 5/28/02				Comment			
				Ultrasound			
	Date	Size	location	Right	Left		
	5/21/02	3.5x1.7x 2.4 cm	RUI 5 cm from nipple				
Manmogram 5/21/02							

Pulse Oximeter

Right hand	Left hand	Heart Rate	02 Sat
X_Index 6/28/02	___Index other___	75_/mins	99_ %
___Index other___	X_Index 7/3/02	74_/mins	98_ %
___Index other___	X_Index 7/8/02	68_/mins	98_ %
X_Index 7/29/02	___Index other___	77_/mins	98_ %

Right Index	Left Index	Heart Rate	02 Sat
X_Index 8/14/02	___Index other___	86_/mins	97_ %
X_Index 9/16/02	___Index other___	78_/mins	100_ %
___Index other___	___Index other___	___/mins	___ %
___Index other___	___Index other___	___/mins	___ %



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March 19, 2003

DAVID JB HSIANG, M.D.
SURGERY

RE: HS# 2002-2306 UCI 02-10: *Monitoring the Response of Chemotherapy on Breast Cancer Tumors by Photon Migration Spectroscopy*

The research project referenced above has been approved by the Institutional Review Board (IRB). Any stipulations of approval imposed by the Committee are recorded below.

Approval of the Institutional Review Board does not, in and of itself, constitute approval for implementation of this project. Other levels of review and approval may be required (e.g., EH&S, Radiation Safety, School Dean). Studies undertaken in conjunction with outside entities, such as drug or device companies, are typically contractual in nature and require an agreement between the University and the company. These agreements must be executed by an institutional official in the UCI Office of Sponsored Projects Administration. The University is not obligated to legally defend or indemnify an employee who individually enters into these agreements and investigators are personally liable for contracts that they sign. Accordingly, the project should not begin until all required approvals have been obtained.

No changes are to be made to either the approved protocol nor the approved, stamped consent form without the prior review and approval of the IRB. Approval for research extends to its performance only at the sites identified in your protocol application. The enclosed consent form with the UCI approval stamp must be used for all human subjects entered into this study. All unanticipated or adverse effects must be reported to the IRB (via Institutional Review Board Administration) in accordance with U.S. Food and Drug Administration regulations and UCI policy.

Approximately 90 days prior to expiration of this approval, you should receive a memo reminding you to apply for continuing review. It is your responsibility to assure current approval of your protocol is maintained throughout the duration of the study.

David Imagawa, M.D., Ph.D., Chair, Institutional Review Board
Approval Issued: 3/19/03 to 3/18/04

UCI has a Human Subjects Federalwide Assurance
(FWA) 00004071, Approved: 1/31/03

☒ Expedited Review 3/19/03
Categories 1b, 4, and 5

cc: Department Chair

Revised 4/98



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April 10, 2002

DAVID J. B. HSIANG, M.D.
SURGERY

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David Imagawa, M.D., Ph.D., Chair, Institutional Review Board
Approval Issued: 4/10/2002 to 4/09/2003

UCI has a Multiple Project Assurance
M-1305, Approved: 2/1/98

☒ Expedited Review 4/10/2002
Categories 1bi, 4, & 5

cc: Department Chair
Revised 4/98

Beckman Laser Institute Lecture Series

5/2002-5/2003

Appendix C

May 2, 2002

"Effects of Mechanical Forces on Signaling Transduction in Endothelial Cells"

Shu Chien

Departments of Bioengineering and Medicine and

The Whitaker Institute of Biomedical Engineering

University of California, San Diego

May 7, 2002

"Optical Noninvasive On-Line Monitoring And Controlling System Based On Nir Absorption Spectroscopy For Glucose Measurement Of Cell Culture Media In Rotary Cell Culture System"

Byungjo Jung, Ph. D.

Texas A&M University

May 9, 2002

"Nanometers and Nanoliters: Science and Technology at the Nanoscale"

Stephen Quake

Dept of Applied Physics

Caltech

May 13, 2002

"Computational Analysis of Integrated Cell Systems"

Daniel Beard, Ph.D.

Research Assistant Professor

Department of Bioengineering

University of Washington

May 16, 2002

"Transport Properties of Spherical Macromolecules in Microfluidic and Physiological Systems"

Dr. Dave Clague

Lawrence Livermore National Lab

June 18, 2002

"The Use of Chemical Agents for the Enhanced Penetration of Light in Biological Tissue: Implications for Light-Based Diagnostics and Therapeutics"

Gracie Vargas, Ph.D.

Department of Biomedical Engineering

University of Texas

July 18, 2002

"Femtosecond Laser Microscopy For Diagnostics And Nanosurgery"

Karsten Koenig

Center for Laser Microsurgery

University Jena

Germany

August 9, 2002

"Non-Invasive Optical Diagnostics of Cartilage"

Jong-In Youn (PhD Candidate)

Department of Biomedical Engineering

The University of Texas at Austin

September 17, 2002

"Microstructure fibers...who ever thought that glass could be this much fun?"

Jay Sharping

Center for Photonic Communications and Computing,

Northwestern University

Evanston, IL

November 13, 2002

"Imaging Skin Microcirculation using the Laser Doppler Technique - Theory and Practice"

Tomas Stromberg, Ph.D.

Associate Professor, Department of Biomedical Engineering

Linkoping University

Linköping, Sweden

November 14, 2002

"Problems Of Coronary Physiology"

Dr. Julien Hoffman

University of California San Francisco

November 21, 2002

"Biomechanical Basis for Esophageal Motor Disorders and Esophageal Sensation"

Dr. Ravi Mittal

University of California San Diego

Beckman Laser Institute Lecture Series

5/2002-5/2003

Appendix C

December 5, 2002

"Toward Replacement Parts for the Brain:
Implantable Biomimetic Electronics as the Next
Era in Neural Prosthetics"
Dr. Ted Berger
University of Southern California

December 9, 2002

"Ultra-High-Stability Er^{3+} Doped Fiber Laser
Sources For Fiber Optic Gyroscopes"
Philippe Zatta, PhD
Post-doctoral research associate
Department of Electrical Engineering
University of Notre Dame, IN

December 12, 2002

"Induction of Programmed Cell Death in Human
Lymphocytes by Ultra-Short Pulsed Electric
Fields"
Martin Gundersen, Ph.D.
Electrical Engineering and Physics
University of Southern California

January 22, 2003

"Tissue Imaging Using Nonlinear Optical
Microscopy"
Alvin Yeh, Ph. D.
Beckman Laser Institute
UCI

February 4, 2003

"From Optical Trapping to Single-Particle
Spectroscopy
& Photonic Force Microscopy for Bio- and
Nano- Applications"
Dr. Arthur Chiou
Professor, EE Department &
Dean, College of Science & Engineering
National Dong Hwa Univ.
Shoufeng, Hualien, Taiwan

February 20, 2003

"Vestibular System, Balance Disorders, and
Opportunities for
MEMS-based Electrostimulatory Vestibular
Prosthesis"
Andrei M. Shkel
Mechanical & Aerospace Engineering
University of California, Irvine

March 5, 2003

"Forward-viewing Ring-Annular Array for
Intravascular Ultrasound Imaging"
Yao Wang, Ph.D.
Biomedical Ultrasound Lab
University of Michigan

March 6, 2003

"Role of Angiogenesis in Ovarian Cancer"
Sundaram Ramakrishnan, Ph.D.
University of Minnesota
Dept. of Pharmacology

March 13, 2003

"Ventricular Assist Devices"
Dan E. Gutfinger, M.D., Ph.D.
University of Arizona Medical Center

March 20, 2003

"Radiofrequency Volumetric Heating of Tissue
with Concomitant Cooling"
Karl Pope, Ph.D.
Director of Research and Development
Thermage Inc., Hayward. CA

April 24, 2003

"Revolution Ahead in Wireless Communications
- A MEMS Perspective"
Norman C. Tien, Ph.D.
Department of Electrical and Computer
Engineering
University of California, Davis

UCI Beckman Laser Institute and Medical Clinic Protocol # 2002-2306

Optical Breast Tissue Study Neoadjuvant

2002	MR#	Consent	Initial	Race	BD	menopausal	Lesion	Type CA	chemo Rx pre-op	Radiation post-op	chemo post-op	Surgery
1	1725549	6/24/2002	CK	asian	10/5/1954	pre-m	RUI	Multicentric Invasive lobular carcinoma	4 Rx		4 Rx	Rt. Breast mastectomy w/ axillary node dissection 9/19/02
2	1728491	7/19/2002	RK	Pakistan	1/20/1947	post-m	LUO	Infiltrating lobular carcinoma, Bloom-richardson score 5/9	8 Rx	35 Rx		bilateral modified radical mastectomy 3/21/03
3	1742493	8/23/2002	SV	asian	7/10/1949	post-m	LUO	invasive poorly differentiated ductal carcinoma	8 Rx	35 Rx		Lt. Lumpectomy 3/27/03
4	1658696	11/19/2002	SA	polynesian	6/10/1955	post-m	RUO	Adenocarcinoma	8 Rx			pending 5/23/03
5	1753460	12/4/2002	RV	hispanic	10/29/1937	post-m	LUO	Infiltrating ductal carcinoma with lobular and signet ring cell features	8 Rx			pending 5/23/03
6	1759566	12/4/2002	AS	hispanic	10/11/2369	post-m	RUO	Infiltrating ductal carcinoma, modified bloom-richardson grad 3/3	8 Rx			
7	1759577	12/5/2002	MG	hispanic	3/14/1964	post-m	RUO	Infiltrating ductal carcinoma, modified bloom-richardson GRAD 3/3	8 Rx			Drop
8	1759670	12/11/2002	OG	hispanic	5/2/1972	pre-m	RUI	Invasive moderately to poorly differentiated GRAD II-III / IV ductal carcinoma	8 Rx			

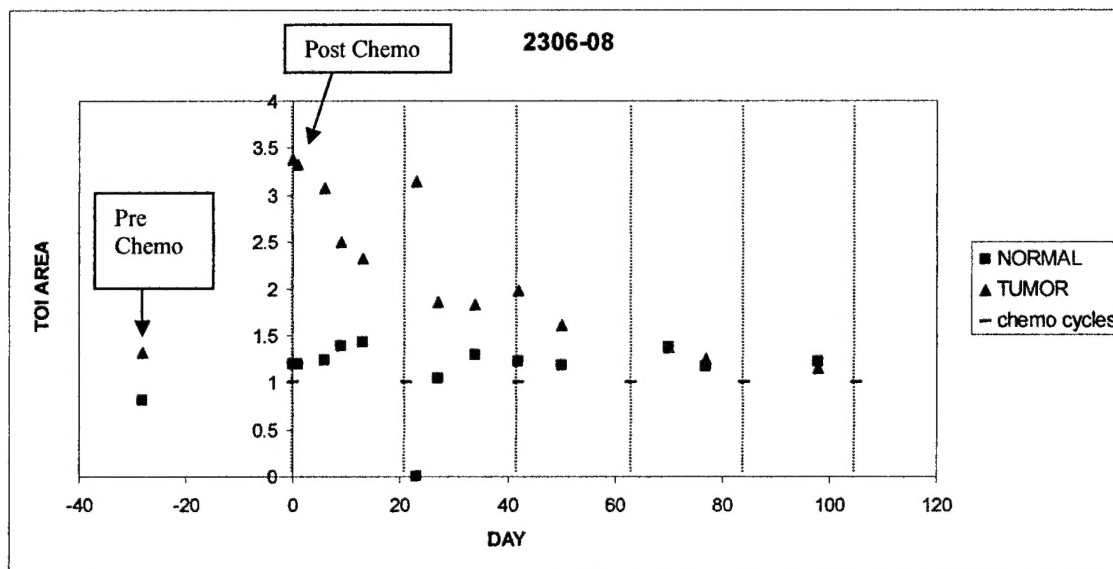
Neoadjuvant study BLS 95-563 / 2002-2306

No	MR#	Consent	Initial	Race	BD	menopausal	Lesion	Pathology	chemo Rx pre-op	Radiation post-op	chemo post-op	Surgery
1	1580410	2.14.02	JB	white	11.21.42	post-m	LLO	Invasive ductal adenocarcinoma	8 Rx	35 fraction	none	Lt. total mastectomy 10/25/02
2	1738410	10.23.02	CS	white	7.23.32	post-m	LUO	Lt. axillary mass show invasive lobular carcinoma	4 Rx	35 Rx	1 Rx	Lt. Lumpectomy 2/13/03
14												
15												
16												
17												
18												
19												
20												
21												

Appendix D

Appendix E

Sample of Preliminary Data



This is a plot of measurements prior to the Pre chemotherapy and Post chemotherapy. One observes a major change in the breast physiology after the first and second cycles of chemotherapy. Then in subsequent cycles the breast physiology changes less. Whereas the normal contra lateral breast remains unchanged (blue square) In all patients the change in breast physiology is greatest in after the first chemotherapy cycle.